REMARKS

Applicants previously canceled Claims 19-30 and 32-74. Applicants have canceled Claim 3 and have amended Claims 1, 4, 7, and 31 for clarity herein. Enabling support for the amendments can be found in the application as filed (*See, e.g.*, original claims and Example 19). Therefore, no new matter is contained in the amendments. Reconsideration of the present application and allowance of pending Claims 1, 2, 4-9, and 31 are respectfully requested in view of the amendments and following remarks.

Applicants also have withdrawn Claims 10-18 herein, as being drawn to a non-elected invention. Applicants note that the claims of Groups I (Claims 1-9 and 31) and II (Claims 10-18) are related as product and process of making the product, respectively. Accordingly, as the product claims are believed to be in condition for allowance, Applicants request rejoinder of Claims 10-18, directed to the non-elected invention. MPEP § 821.04(b). In addition, Applicants elected the species of a trisomy of chromosome 17. As the claims are believed to be in condition for allowance as they relate to the elected species, Applicants request that the Patent Office examine the claims as they relate to the non-elected species which are written in dependent form or otherwise include all of the limitations of the allowable generic claim as provided by 37 C.F.R. § 1.141. Consideration and allowance of Claims 10-18 are respectfully requested.

I. Restriction Requirement

The Office Action made final the previous restriction requirement. Accordingly, Applicants have withdrawn Claims 10-18 herein, as being drawn to a non-elected invention. However, as noted above, because the claims of Group I (Claims 1-9 and 31, related to a product) are believed to be in condition for allowance, Applicants respectfully request rejoinder of Claims 10-18 (Group II, related to processes for making the product of Group I).

In addition, Applicants elected the species of a trisomy of chromosome 17. As the claims are believed to be in condition for allowance as they relate to the elected species, Applicants respectfully request that the Patent Office examine the pending claims as they relate to the non-elected species at this time.

II. Priority

The Office Action alleged that the priority application (Provisional Application No. 60/459,090) fails to provide adequate support or enablement in the manner provided by 35 U.S.C. § 112, first paragraph, for Claims 3-9. In particular, the Office Action noted that the priority application does not include Example 19 or a disclosure of the abnormal karyotypes in bulk passaged human ES cells. Therefore, the Office Action indicated that Claims 3-9 are only entitled to the priority date of March 31, 2004, the filing date of the PCT application.

Applicants respectfully submit that the currently pending claims as amended are sufficiently supported and enabled by Provisional Application No. 60/459,090. For example, the specification describes the SSEA4 selection and bulk passaging of cells with trypsin treatment at Example 6 of the provisional application, paragraphs [0142]-[0146] and Example 11, [0175]-[0178]. Undifferentiated human ES cells were selected by magnetic sorting using an anti-SSEA4 antibody and then passaged with trypsin treatment to dissociate the culture to an essentially single cell suspension. This cell population inherently has the characteristic of having an abnormal karyotype as a result of this passaging technique. Accordingly, as the provisional application discloses this passaging technique that produces cells that have an abnormal karyotype, the currently pending claims are entitled to the benefit of the priority date of the provisional application filing date.

III. Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-9 and 31 were rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Office Action asserted that Claims 1 and 31 are directed to a mixed culture of cells undergoing differentiation. The Office Action asserted that the specification teaches that the cells that do not express SSEA1 and do express SSEA3, SSEA4, Oct4, Tra-1-60, Tra-1-80, and nestin are not pluripotent cells, but rather are differentiating cells present in embryoid bodies that are committed to a neural differentiation path.

Applicants respectfully submit that this rejection is moot with respect to the currently pending claims. The invention is not directed to differentiated cells or even a mixture of differentiated and undifferentiated cells, but rather the invention is directed to aneuploid ES cells that are produced as a result of bulk passaging with trypsin treatment. The claims have been amended to clarify that the claimed cell culture is an "aneuploid embryonic stem cell culture" as is produced by the described passaging technique. The currently pending claims particularly point out and distinctly claim the subject matter of the invention. Therefore, the rejection under 35 U.S.C. § 112, second paragraph should be withdrawn.

IV. Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-9 and 31 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. In particular, the Office Action alleged that the specification is not enabling for a human pluripotent stem cell culture wherein the cells do not express SSEA-1, and do express SSEA3, SSEA4, Oct4, Tra-1-60, Tra-1-80, and nestin substantially uniformly. The Office Action alleged that the embryoid body cells analyzed for cell surface marker expression are a mixed cell population and that the specification does not demonstrate that such cells retain the ability to differentiate into all cell lineages. Applicants respectfully submit that the specification is sufficient to enable one of ordinary skill in the art to make and use the present invention without undue experimentation.

As discussed above, the presently claimed invention is not directed to differentiated cells or even a mixture of differentiated and undifferentiated cells, but rather the claimed invention is directed to aneuploid ES cells that are produced as a result of bulk passaging with trypsin treatment. The claims have been amended to clarify that the claimed cell culture is an "aneuploid embryonic stem cell culture." The specification describes human ES cells that were selected by selecting cells that express SSEA4 and bulk passaging using trypsin treatment (*e.g.*, Example 6 and 11). These cells inherently have an abnormal karyotype, and this trait was confirmed in Example 19. Therefore, the specification clearly enables one of ordinary skill in the art to make the present invention without exercising undue experimentation.

In addition, the Office Action alleged that the claimed invention is not useful if the pluripotent human ES cells are karyotypically abnormal. Applicants respectfully submit that the claimed human ES cells have utility. For example, the claimed cells can be used to study cancer and early transforming genetic events leading to tumorigenesis. The attached review states that karyotypic changes are indicators of tumorigenesis (*See* Baker *et al.*, 2007, Nature Biotechnol. 25(2):207-15). Accordingly, the selection of karyotypically abnormal cells using the presently disclosed passaging technique is useful for studying early transforming genetic events leading to tumorigenesis.

The specification is sufficient to enable one of ordinary skill in the art to make and use the invention as in the currently pending claims without exercising undue experimentation. Therefore, the rejection under 35 U.S.C. § 112, first paragraph with respect to the enablement requirement should be withdrawn.

V. Rejections under 35 U.S.C. § 102

A. The Office Action rejected Claims 1, 2, and 31 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,833,269 to Carpenter *et al.* Applicants respectfully submit that Claims 1, 2, and 31 are novel over the teachings of Carpenter *et al.*

The Office Action asserted that Carpenter *et al.* teach populations of human ES cells and neural progenitor cells by culturing, expanding, and differentiating ES cells into a variety of different neural phenotypes under different growth conditions. The Office Action asserted that the cells were expanded by serial passaging, removed, and used in the formation of embryoid bodies. The Office Action further asserted that Carpenter *et al.* teach that the differentiation of primate ES cells results in a loss of expression of SSEA3, SSEA4, Tra-1-60, and Tra-1-80, and an increase in expression of SSEA-1. The Office Action also asserted that Carpenter *et al.* teach that Oct-4 expression is a characteristic of undifferentiated hES cells and that nestin expression is a characteristic of neural precursor cells. The Office Action asserted that Carpenter *et al.* also teach the single cell suspension of neural stem cells. Accordingly, the Office Action concluded that Carpenter *et al.* anticipate the present invention.

A claim is anticipated only when a single prior art reference expressly or inherently teaches each and every feature of the claim. *See Verdegaal Bros. v. Union Oil Co. of Cal.*, 814 F.2d 628 (Fed. Cir. 1987). Carpenter *et al.* do *not* teach each and every feature of the presently claimed invention. The currently pending claims are directed to an "aneuploid human embryonic stem cell" culture wherein the cells do not express SSEA1, and do express SSEA3, SSEA4, Tra-1-60, Tra-1-80, and nestin. Carpenter *et al.* do not teach the claimed *aneuploid* human ES cells. In fact, Carpenter *et al.* teach away from the present invention, teaching *differentiated* cells and teaching neural progenitor cells for use in the treatment of various diseases which cause acute or chronic damage to the central nervous system (Col. 9, lines 27-52). While Carpenter *et al.* do in fact list various markers as being characteristic of differentiated or undifferentiated cells (Col. 11 and 14), Carpenter *et al.* do *not* disclose cells that have the presently claimed features, *i.e.*, cells that are aneuploid, that do not express SSEA1, and that do express SSEA3, SSEA4, Tra-1-60, Tra-1-80, and nestin. In addition, as the Examiner noted in the Office Action that cells with abnormal karyotypes are to be avoided in the potential use as therapeutics, Carpenter *et al.* arguably teach away from the presently claimed cells with abnormal karyotypes.

Carpenter *et al.* do not teach each and every feature of the presently claimed invention. Therefore, Carpenter *et al.* do not anticipate the present invention, and the rejection under 35 U.S.C. § 102(e) should be withdrawn.

B. The Office Action rejected Claim 31 under 35 U.S.C. § 102(b) as allegedly being anticipated by Odorico *et al.* (2001, Stem Cells 19:193-204) Applicants respectfully submit that Claim 31 is novel over the teachings of Odorico *et al.*

The Office Action asserted that Odorico *et al.* teach human pluripotent stem cells that can differentiate into derivatives of all three embryonic germ layers. The Office Action asserted that Odorico *et al.* teach that human ES cells express SSEA3 and SSEA4, Tra-1-60, and Tra-1-81, and that in suspension culture, human ES cells differentiate into embryoid bodies and can further differentiate into a variety of cell types, including neural cells. Accordingly, the Office Action concluded that Odorico *et al.* anticipate the present invention.

Odorico *et al.* do not teach each and every feature of the presently claimed invention. As noted above, the currently pending claims are directed to an "aneuploid human embryonic stem

cell" culture wherein the cells do not express SSEA1, and do express SSEA3, SSEA4, Tra-1-60, Tra-1-80, and nestin. Odorico *et al.* list various markers as being characteristic of undifferentiated cells, *e.g.*, SSEA3 and SSEA4, Tra-1-60, and Tra-1-81, but Odorico *et al.* do not teach the expression of this combination of these markers with nestin on a single cell. Further, Odorico *et al.* do not teach cells that are aneuploid. Odorico *et al.* teach that human ES cells have "remarkably stable karyotypes" (Page 195, 1st column, 3rd full paragraph). Therefore, Odorico *et al.* arguably teach away from the presently claimed ES cells with abnormal karyotypes.

Odorico *et al.* do not teach each and every feature of the presently claimed invention. Accordingly, Odorico *et al.* do not anticipate the present invention, and the rejection under 35 U.S.C. § 102(b) should be withdrawn.

CONCLUSION

Applicants believe that the present application, as amended, is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The foregoing is submitted as a full and complete response to the Office Action mailed July 25, 2007.

No fees are believed due at this time. However, please charge any fees that may be due, or credit any overpayment, to Deposit Account 19-5029 (Ref. No.: 18377-0067). In addition, if there are any issues that can be resolved by a telephone conference or an Examiner's amendment, the Examiner is invited and encouraged to call the undersigned attorney at (404) 853-8000.

Respectfully submitted,

Kathryn H. Wade

By: Kathryn H. Wade, Ph.D.
Reg. No. 54,682
Attorney for Applicant

SUTHERLAND ASBILL & BRENNAN LLP
999 Peachtree Street, NE
Atlanta, Georgia 30309-3996
(404) 853-8000
SAB Docket: 18377-0067